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Relationships between Crystallinity of β-Cyclodextrin and Tablet Characteristics

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The effects of the crystallinity of β-cyclodextrin (β-CD) on the hardness, apparent density and disintegration time of β-CD tablet have been studied. β-CD powders with various degrees of crystallinity were prepared by grinding and used for tableting. The crystallinity was measured by the X-ray diffraction method. Linear relationships were found between tablet compression force and tablet hardness. It was also observed that decreasing crystallinity caused an increase of tablet hardness as well as disintegration time. The results indicate that crystallinity is one of the important factors controlling tablet characteristics.

Keywords——cyclodextrin; crystallinity; tablet hardness; disintegration; X-ray diffraction; compression

In previous papers, we reported the crystallinity changes of microcrystalline cellulose, lactose and β-cyclodextrin (β-CD) caused by grinding.[2)] Crystallinity is an important parameter of pharmaceutical solids.[3)] Although changes of crystallinity may have marked influences on tablet characteristics, few reports have been published on the significance of the effect.[4–6)] We therefore examined the effects of crystallinity on the hardness, apparent density and disintegration time of compacted β-CD powders.

Experimental

Materials——β-CD (original) was obtained from Ando Kasei Co. β-CD hydrate was recrystallized from water. Water content of β-CD powders was measured by the Karl Fisher method as 14.8%. A vibrational mill (Chuokakoki, type B1) was used to obtain ground β-CD powders.[2a)]

X-Ray Diffraction Measurement and Crystallinity Determination——Powder X-ray diffraction patterns were measured as previously described.[2c)] Crystallinity was calculated according to Ruland's method with some modification.[2c)]

Tablet Studies——β-CD powder (250 mg, 74—177 μm in particle diameter) was compacted in a hydraulic press (Riken Powder, P-1B), using a flat faced punch with a diameter of 9.5 mm. The compression pressure was 30—220 kg/cm^2. The punch and die were wiped with magnesium stearate to reduce die friction. Tablet hardness was measured with an Erweka hardness tester. For calculation of the apparent density of a tablet, the tablet thickness was measured with vernier calipers to a precision of 0.05 mm. A tablet disintegration apparatus (JP X) was used to determine the disintegration time in a water at 37 °C. The experiments were carried out 5 times under each set of conditions.

Results and Discussion

Table I shows the crystallinity and disorder parameter of β-CD powders. Recrystallization from water increased the crystallinity of β-CD, while grinding decreased it. X-Ray diffraction peaks due to β-CD crystals were not observed in a sample ground for 15 min.

TABLE I. Crystallinity and Disorder Parameter of β-Cyclodextrin

β-Cyclodextrin	Crystallinity (%)	Disorder parameter (Å²)
Hydrate	85.9	4.3
Original	62.8	4.7
2 min ground	32.6	5.0
5 min ground	8.7	5.8
15 min ground	0	—

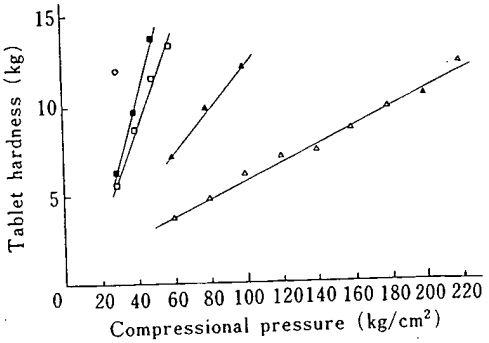

Fig. 1. Relationship between Hardness and Compressional Pressure for Directly Compressed Tablets of Various Forms of β-Cyclodextrin

△, hydrate; ▲, original; □, ground for 2 min; ■, ground for 5 min; ○, ground for 15 min.

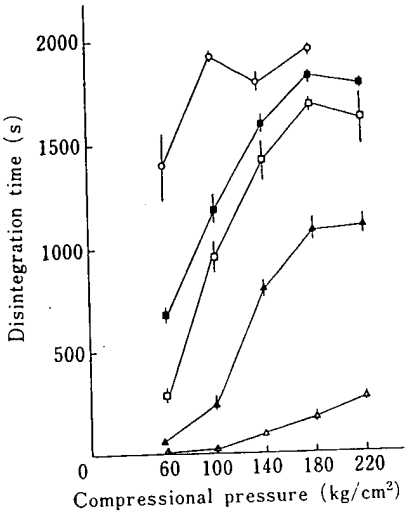

Fig. 2. Relationship between Disintegration Time and Compressional Pressure for Directly Compressed Tablets of Various Forms of β-Cyclodextrin

Each bar shows the standard deviation.
△, hydrate; ▲, original; □, ground for 2 min; ■, ground for 5 min; ○, ground for 15 min.

TABLE II. Apparent Densities (g/cm³) of β-Cyclodextrin at Different Compressional Pressures

Crystallinity of β-cyclodextrin (%)	Compressional pressure (kg/cm²)				
	60	100	140	180	220
85.9	1.21	1.28	1.33	1.35	1.36
62.8	1.12	1.23	1.30	1.29	1.33
32.6	1.13	1.23	1.30	1.33	1.35
8.7	1.10	1.18	1.25	1.27	1.31
0	1.20	1.30	1.34	1.34	—

The powders were compacted after sieving and the hardness was measured as shown in Fig. 1. Linear relationships were found between tablet hardness and compressional pressure, except in the case of the 15 min ground sample, whose hardness was too large to measure. It was observed that the hardness increased in the following order; recrystallized

powder < original powder < 2 min ground sample < 5 min ground sample < 15 min ground sample. This is the reverse of the order of their crystallinities, that is, decreasing crystallinity caused an increase in tablet hardness. Table II shows the apparent tablet density measured immediately after ejection. The 15 min ground sample had a higher density than the original sample or the 2 min or the 5 min ground sample. The increase in apparent density of the 15 min ground sample may be attributed to one or more of the following effects: (1) difference of transmission of the compacting pressure, (2) change of particle shape, (3) decrease of intraparticular voids. It should be possible to obtain further useful information on the apparent density by more detailed investigation. The disintegration times of tablets prepared at five different compressional pressures are shown in Fig. 2. A significant correlation between β-CD crystallinity and disintegration time was found, as observed in the case of tablet hardness. At short disintegration times (less than about 700 s), the disintegration took place after water permeation into the tablet capillaries and the swelling of β-CD.[5] However, in the case of the tablets showing longer disintegration times, β-CD dissolution from the tablet surface was the rate-determining process for the disintegration, and the disintegration time showed less dependence on compressional pressure.

Nakai *et al.* have investigated the effect of microcrystalline cellulose[2a] and lactose[4] crystallinity on the tablet characteristics. Different effects of crystallinity on the tablet hardness were reported in these cases, that is, decrease of crystallinity decreased the tablet strength for microcrystalline cellulose and increased it for lactose (as was the case with β-CD). On the other hand, a longer disintegration time was observed for the tablets made from amorphous microcrystalline cellulose.

These results indicate that crystallinity has an important effect on the properties of compressed powder.

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References and Notes

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2) *a*) Y. Nakai, E. Fukuoka, S. Nakajima and J. Hasegawa, *Chem. Pharm. Bull.*, **25**, 96 (1977); *b*) Y. Nakai, E. Fukuoka, S. Nakajima and M. Morita, *ibid.*, **30**, 1811 (1982); *c*) Y. Nakai, K. Yamamoto, K. Terada and A. Kajiyama, *Yakugaku Zasshi*, **105**, 580 (1985).
3) M. Morita and S. Hirota, *Chem. Pharm. Bull.*, **33**, 2091 (1985).
4) M. Morita, Y. Nakai, E. Fukuoka and S. Nakajima, *Chem. Pharm. Bull.*, **32**, 4076 (1984).
5) H. Maekawa, "Pharmaceutical Technology," ed. by K. Tsuda and H. Nogami, Chijin Syokan, Tokyo, 1971, pp. 167—170.
6) R. Hüttenrauch and I. Keiner, *Pharmazie*, **31**, 331 (1976).